修士論文要旨

Zinc-deficiency and its recovery responses on the distribution of granulocytes, and thermogenesis in rats

Yuko Sakakibara Director : Kazuhiko Imaizumi

Introduction : Zinc (Zn) is one of the essential trace elements for all organisms, and is second in abundance to iron in the body. In human, Zn is a cofactor for more than 300 enzymes. It is well known that these Zn containing enzymes are shown to regulate growth, acid-base equi -librium state and oxygen transport functions. However, the effects of Zn on the immune system remain relatively unknown. In *Exp. 1*, we studied the effects of the Zn -deficiency and its recovery on the distribution of the number of total white blood cells (WBCs), neutrophil, eosinophil, and basophil in rats. As a result, Zn-defi -ciency induced stress responses that accorded with the promotion of the hypothalamus-pituitary-adrenal stress (HPA) axis. In addition to stress response, Zn-defi -ciency also induce low metabolism. Thus, the effects of Zn on the thermogenesis remain unknown. In *Exp. 2*, we investigated the effects of Zn-deficiency and its re -covery on the rectal temperature, an index of deep body thermogenesis in weaned male rats.

Materials and Methods : 3 week old Sprague-Dawley male rats were divided into the Zn-deficient diet (ZDF: 0.6mg Zn/kg diet) group and the control diet (CON: 35.2mg Zn/kg diet) group, and were pair-fed for 4 wks (Zn-deficiency). After 4 wks, both groups were pair fed with the control diet for 3 wks (recovery). Blood samples were collected from tail vein. The number of WBCs, plasma Zn and corticosterone concentrations were ana -lyzed by flow-cytometry, spectrophotometry and ELISA, respectively[1]. Rectal temperatures of rats were measured with a thermister probe at 10:30-11:30 AM[2]. These studies were approved by the Animal Ethics Committee, Waseda University (10J013).

Results and Discussion : Plasma Zn and corticosterone concentrations were clearly lower and higher in ZDF group than in CON group during Zn-deficiency, however, those were recovered to CON group levels during re -covery (data not shown)[1]. As shown as Fig. 1, the number of neutrophil (A), eosinophil (B) and basophil (C) during Zn-deficient was clearly higher in ZDF group than in CON group, respectively. The number of granulocytes in ZDF group in 1-2 weeks of recovery was recovered to CON group levels. Especially, the rate of recovery in the number of basophil was higher than other granulocytes, and the number was promptly recovered to CON group levels for 1 week. These results suggest that the innate immune responses and stress responses were at least in part involved in Zn-deficiency and its recovery[1]. As shown as Fig.1D, the rectal temperature in weeks 1-4 of Zn-deficiency was clearly lower in ZDF group than in CON group. However, the rectal temperature in ZDF group was recovered to CON group levels in week 1 of recovery. These results suggest that hypothermia was induced at least after 1 week of Zn-deficiency, was re -covered to the basal levels at least in 1 week of recovery, and its recovery responses are reversible[2].

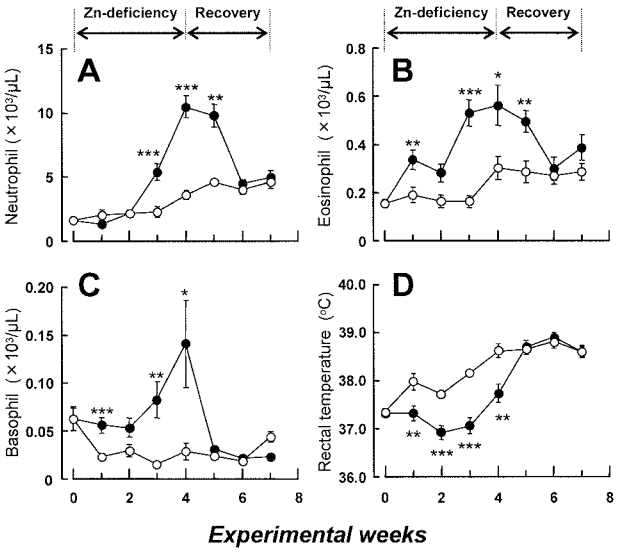

Fig. 1 Effects of Zn-deficiency and its recovery on the number of granulocytes (A-C), rectal temperature (D). Means±SE. ○: CON group and ●: ZDF group. $*p<0.05$, $**p<0.01$ and $***p<0.001$ (vs. CON group, two-way ANOVA).

References : 1) Sakakibara Y, Sato S, *et al., J Nutr Sci Vitaminol,* 57: 197-201 (2011); 2) Sakakibara Y, Sato S, *et al., J Toxicol Sci,* 36: 681-685 (2011).